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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,915	09/24/2003	Richard Daifuku	021227-000310US	6525

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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,915	DAIFUKU ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted September 5, 2008 wherein claim 1 is amended. This application claims benefit of provisional application 60/41337, filed September 24, 2002.

Claims 1 and 8-15 are pending in this application.

Claims 1 and 8-15 as amended are examined on the merits herein.

The declaration of Kevin Harris, submitted September 5, 2008 under 37 CFR 1.132 has been fully considered and entered into the record. The declaration is discussed further below as it relates to the rejections of record in the previous office action.

Applicant's amendment and arguments, submitted September 5, 2008, with respect to the rejection of claims 9 and 11 under 35 USC 112, second paragraph for indefinitely reciting "a cell" without specifying what cell is cleaving the compound, have been fully considered and found to be persuasive to remove the rejection as one skilled in the art would interpret the scope of the claims to apply to any cell to which the compound is administered. Therefore the rejection is withdrawn.

Applicant's amendment and the declaration of Kevin Harris, submitted September 5, 2008, with respect to the rejection of instant claim 1 under 35 USC 103(a) for being obvious over Powell et al., have been fully considered and found to be

persuasive to remove the rejection as the claims have been amended to require that R^4 be hydrogen. Therefore the rejection is withdrawn.

Applicant's amendment and the declaration of Kevin Harris, submitted September 5, 2008, with respect to the rejection of instant claims 12-15 under 35 USC 103(a) for being obvious over Powell et al. in view of Cullis et al., have been fully considered and found to be persuasive to remove the rejection as the claims have been amended to require that R^4 be hydrogen. Therefore the rejection is withdrawn.

Applicant's amendment and the declaration of Kevin Harris, submitted September 5, 2008, with respect to the rejection of instant claims 10 and 11 under 35 USC 103(a) for being obvious over Powell et al. in view of McGuigan et al., have been fully considered and found to be persuasive to remove the rejection as the claims have been amended to require that R^4 be hydrogen. Therefore the rejection is withdrawn.

Applicant's amendment and the declaration of Kevin Harris, submitted September 5, 2008, with respect to the rejection of instant claims 8 and 9 under 35 USC 103(a) for being obvious over Powell et al. in view of McGuigan et al. 2, have been fully considered and found to be persuasive to remove the rejection as the claims have been amended to require that R^4 be hydrogen. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Skulnick. (US patent 4171431, cited in PTO-1449)

Skulnick discloses 5,6-dihydro-triazine deoxynucleosides having a structure anticipating the structure of instant claim 1. (column 2 lines 20-69, the embodiment where in Y-H or phosphono, Y' = H, X = NH or N-alkyl, Z = O, R = H or C2-C4 alkyl, and R' = H) These compounds are active *in vivo* against susceptible DNA viruses. (column 4 lines 52-63) Therefore Skulnick anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skulnick (Reference cited in PTO-1449) as applied to claim 1 above, and further in view of Cullis et al. (US patent 6852334, of record in previous action) the disclosure of Skulnick is discussed above. Skulnick does not disclose a composition further comprising an amphiphilic species and a dendrimeric polyamine according to instant claims 12-15.

Cullis et al. discloses conjugates that can be incorporated into stabilized plasma lipid particles comprising a lipid anchor, a non-immunogenic polypeptide, and a polycationic moiety, and further comprising a bioactive agent and a second lipid. (column 2 line 33 – column 3 line 23) The polycationic moiety can have between 2-15 positive charges, derived from basic amino acids or amines, for example tetralysine, as well as polycationic dendrimers. (column 13 lines 17-32) These polycations thus include compounds reasonably considered to be polyamines, and one of ordinary skill in the art would recognize polyamine dendrimers as being another useful embodiment of this species. These conjugates are incorporated into lipid-based drug formulations such as liposomes, composed of specific lipids such as phospholipids which are considered to be composed of a hydrophobic domain and a hydrophilic domain covalently bound to one another. (column 16, lines 11-34) These liposome formulations are useful for delivering bioactive agents such as antineoplastic agents and nucleoside analogs. (column 21 lines 29-60) The formulations are preferably delivered as an aqueous intravenous solution. (column 24 lines 52-60)

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the dihydro-azacytidine compounds of Skulnick in a formulation containing the liposomes and conjugates of Cullis et al. One of ordinary skill in the art would have been motivated to deliver the drugs in this manner because Cullis et al. discloses a method for delivering nucleoside analogs, which would be recognized by one of ordinary skill in the art as including the dihydro-5-azacytidine analogs of Skulnick. One of ordinary skill in the art would reasonably have expected success because

formulating a specific known drug in a specific known drug delivery formulation is well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skulnick (Reference cited in PTO-1449) as applied to claim 1 above, and further in view of McGuigan et al. (Reference U of record in previous action) the disclosure of Skulnick is discussed above. Skulnick does not disclose a compound wherein R^6 is as recited in claims 10 and 11.

McGuigan et al. discloses bis(2,2,2-trichloroethyl) phosphate derivatives of AZT showing enhanced membrane penetration and being able to be hydrolyzed to the active phosphate *in vivo*. (p. 355, right column, first paragraph, p. 356 figure 1) These compounds exert an anti-HIV effect by being cleaved intracellularly and trapped inside of the target cell. (p. 357, right column, last paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the compounds of Skulnick with a bis(2,2,2-trichloroethyl) phosphate group as disclosed by McGuigan et al. One of ordinary skill in the art would have been motivated to make this substitution because McGuigan et al. discloses that the bis(2,2,2-trichloroethyl) phosphate group is a prodrug that releases nucleosides intracellularly, and Skulnick already discloses phosphorylated nucleosides. One of ordinary skill in the art would reasonably have expected success because McGuigan et

al. already discloses that this approach works when applied to AZT, a deoxynucleoside analog of similar structure.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skulnick (Reference cited in PTO-1449) as applied to claim 1 above, and further in view of McGuigan et al. 2 (Reference V of record in previous action) the disclosure of Skulnick is discussed above. Skulnick does not disclose a compound wherein R^6 is as recited in claims 10 and 11.

McGuigan et al. 2 discloses an aryl (2,2,2-trichloroethyl) phosphate derivative of AZT showing enhanced membrane penetration and being able to be hydrolyzed to the active phosphate *in vivo*. (p. 312, first and second paragraphs and figure 1, p. 313 first paragraph) These compounds exert an anti-HIV effect by being cleaved intracellularly and trapped inside of the target cell. (p. 317, last paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the compounds of Skulnick with an aryl (2,2,2-trichloroethyl) phosphate group as disclosed by McGuigan et al. 2. One of ordinary skill in the art would have been motivated to make this substitution because McGuigan et al. 2 discloses that the an aryl (2,2,2-trichloroethyl) phosphate group is a prodrug that releases nucleosides intracellularly, and Skulnick already discloses phosphorylated nucleosides. One of ordinary skill in the art would reasonably have expected success

because McGuigan et al. 2 already discloses that this approach works when applied to AZT, a deoxynucleoside analog of similar structure.

Therefore the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
11/21/2008

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623